

Claims

1. A pharmaceutical composition comprising at least one compound capable of enhancing gap-junction communication and at least one nucleoside analogue.

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2. The composition of claim 1, wherein said compound capable of enhancing gap-junction communication is an aromatic organic acid, a pharmaceutically acceptable salt or an ester or amide of said acid.

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3. The composition of claim 2, wherein said aromatic organic acid is a compound of the formula:



wherein R_0 is aryl (e.g., phenyl, napthyl), phenoxy, substituted aryl (e.g., one or more halogen [e.g., F, Cl, Br, I], lower alkyl [e.g., methyl, ethyl, propyl, butyl] or hydroxy substituents) or 15 substituted phenoxy (e.g., one or more halogen [e.g., F, Cl, Br, I], lower alkyl [e.g., methyl, ethyl, propyl, butyl] or hydroxy substituents);

R_1 and R_2 are each H, lower alkoxy (e.g., methoxy, ethoxy), lower straight and branched chain alkyl (e.g., methyl, ethyl, propyl, butyl) or halogen (e.g., F, Cl, Br, I);
 R_3 and R_4 are each H, lower straight and branched chain alkyl (e.g., methyl, ethyl, propyl, butyl), lower alkoxy (e.g., methoxy, ethoxy) or halogen (e.g., F, Cl, Br, I); and
20 n is an integer from 0 to 2;
salts thereof (e.g., Na^+ , K^+ or other pharmaceutically acceptable salts); stereoisomers thereof; and mixtures thereof.

25 4. The composition of claim 2, wherein R_0 =aryl, phenoxy, substituted aryl or substituted phenoxy;
 R_1 and R_2 =H, lower alkoxy, lower straight and branched chain alkyl or halogen;
 R_3 and R_4 =H, lower alkoxy, lower straight and branched chain alkyl or halogen; and
20 n =an integer from 0 to 2;
salts thereof; stereoisomers thereof; and mixtures thereof.

5. The composition of claim 3, wherein said aromatic fatty acid is selected from the group consisting of phenylacetic acid, phenylpropionic acid, phenylbutyric acid, 1-naphthylacetic acid, phenoxyacetic acid, phenoxypropionic acid, phenoxybutyric acid,
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4-chlorophenylacetic acid, 4-chlorophenylbutyric acid, 4-iodophenylacetic acid, 4-iodophenylbutyric acid, α -methylphenylacetic acid, α -methoxyphenylacetic acid, α -ethylphenylacetic acid, α -hydroxyphenylacetic acid, 4-fluorophenylacetic acid, 4-fluorophenylbutyric acid, 2-methylphenylacetic acid, 3-methylphenylacetic acid, 4-methylphenylacetic acid, 3-chlorophenylacetic acid, 3-chlorophenylbutyric acid, 2-chlorophenylacetic acid, 2-chlorophenylbutyric acid and 2,6-dichlorophenylacetic acid,
10 and the sodium salts of the these compounds.
6. The composition of claim 5, wherein the aromatic organic acid is 4-Phenylbutyrate or a pharmaceutically acceptable prodrug thereof.
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7. The composition of claim 2, wherein the aromatic organic acid is 2-Phenylbutyrate or a pharmaceutically acceptable prodrug thereof.
8. The composition of claim 5, wherein the aromatic organic acid is phenylacetic acid or a
20 pharmaceutically acceptable salt or an ester of phenylacetic acid.
9. The composition of claim 1, wherein the compound capable of enhancing gap-junction communication is valproic acid, a pharmaceutically acceptable salt thereof or a prodrug of valproic acid.
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10. The composition of claim 1, wherein the compound capable of enhancing gap-junction communication is splitomicin, a pharmaceutically acceptable salt thereof or a prodrug of splitomicin.
- 30 11. The composition of claim 1, wherein the compound capable of enhancing gap-junction communication is butyric acid, a pharmaceutically acceptable salt thereof or a prodrug of butyric acid.
- 35 12. The composition of any of the preceding claims, further comprising a source of deoxyribonucleoside kinase.

13. The composition of claim 12, wherein the source of deoxyribonucleoside kinase is a gene therapy vector.

14. The composition of claim 13, wherein the gene therapy vector is a virus vector.

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15. The composition of claim 14, wherein the virus vector is selected from the group consisting of being a viral vector, in particular a *Herpes simplex* viral vector, an adenoviral vector, an adenovirus-associated viral vector, a lentivirus vector, a retroviral vector or a vaccinia viral vector.

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16. The composition of claim 15, wherein the source of deoxyribonucleoside kinase comprises a composition of packaging cells capable of producing an infective virion comprising said virus vector.

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17. The composition of claim 13, wherein the gene therapy vector is a plasmid vector.

18. The composition of claim 17, wherein the plasmid vector is selected from the group consisting of general eukaryotic expression vectors, vectors for stable and transient expression and epitag vectors as well as their TOPO derivatives for fast cloning of desired inserts.

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19. The composition of claim 12, wherein the source of deoxyribonucleoside kinase comprises a protein formulation.

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20. The composition of claim 19, wherein the protein is formulated as a liposome composition.

21. The composition of claim 12, wherein the source of deoxyribonucleoside kinase comprises a composition of human stem cells genetically engineered to express a heterologous deoxyribonucleoside kinase.

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22. The composition of claim 21, wherein the stem cells used in a stem cell-mediated therapy approach originates from the same tissue as the tumor cells or the same growth layer or alternatively originates from the bone marrow.

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23. The composition of claim 12, wherein the source of deoxyribonucleoside kinase comprises a composition of human progenitor or precursor cells genetically engineered to express a heterologous deoxyribonucleoside kinase.

5 24. The composition according to any of the preceding claims 12 to 21, wherein the deoxyribonucleoside kinase is selected from the group consisting of

10 a. a deoxyribonucleoside kinase having the amino acid sequence of any of SEQ ID No 1 to 17;

 b. a deoxyribonucleoside kinase variant comprising an amino acid sequence having at least 50% sequence identity to any of SEQ ID No 1 to 17; and

 c. a deoxyribonucleoside kinase encoded by a nucleotide sequence capable of hybridising under conditions of high stringency to a nucleotide sequence encoding any of SEQ ID No 1 to 17.

15 25. The composition the deoxyribonucleoside kinases comprise a deoxyribonucleoside kinase selected from the group consisting of

 a. a deoxyribonucleoside kinase having the amino acid sequence of any of SEQ ID NO 1 to 5; and

 b. a deoxyribonucleoside kinase variant comprising an amino acid sequence having at least 70% sequence identity to any of SEQ ID No 1 to 5 and having dNK activity.

20 26. The composition according to any of the preceding claims, wherein the nucleoside analogue is selected from the group consisting of aciclovir (9-[2-hydroxy-ethoxy]-methyl-guanosine), buciclovir, famciclovir, ganciclovir (9-[2-hydroxy-1-(hydroxymethyl)ethoxyl-methyl]-guanosine), penciclovir, valciclovir, trifluorothymidine, AZT (3'-azido-3'-thymidine), AIU (5'-iodo-5'-amino-2',5'-dideoxyuridine), ara-A (adenosine-arabinoside; Vivarabine), ara-C (cytidine-arabinoside), ara-G (9-beta-D-arabinofuranosylguanine), ara-T, 1-beta-D-arabinofuranosyl thymine, 5-ethyl-2'-deoxyuridine, 5-ido-5'-amino-2,5'-dideoxyuridine, 1-[2-deoxy-2-fluoro-beta-D-arabinofuranosyl]-5-iodouracil, idoxuridine (5-ido-2'-deoxyuridine), fludarabine (2-Fluoroadenine 9-beta-D-Arabinofuranoside), gencitabine, 3'-deoxyadenosine (3-dA), 2',3'-dideoxyinosine (ddI), 2',3'-dideoxycytidine (ddC), 2',3'-dideoxythymidine (ddT), 2',3'-dideoxyadenosine (ddA), 2',3'-dideoxyguanosine (ddG), 2-chloro-2'-deoxyadenosine (2CdA), 5-fluorodeoxyuridine, BVaraU ((E)-5-(2-bromovinyl)-1-beta-D-arabinofuranosyluracil), BVdu (5-bromovinyl-deoxyuridine), FIAU (1-(2-deoxy-2-fluoro-beta-D-arabinofuranosyl)-5-iodouracil), 3TC (2'-deoxy-3'-thiacytidine), dFdC

gemcitabine (2',2'-difluorodeoxycytidine), dFdG (2',2'-difluorodeoxyguanosine), 5-fluorodeoxyuridine (FdUrd), d4T (2',3`didehydro-3`-deoxythymidine), ara-M (6-methoxy purinearabinonucleoside), IudR (5-Jodo-2`deoxyuridine), CaFdA (2-chloro-2-ara-fluoro-deoxyadenosine), ara-U (1-beta-D-arabinofuranosyluracil), FBVAU (E)-5-(2-bromovinyl)-1-(2-deoxy-2-fluoro-beta-D-arabinofuranosyl)uracil, FMAU 1-(2-deoxy-2-fluoro-beta-D-arabinofuranosyl)-5-methyluracil, FLT 3'-fluoro-2'-deoxythymidine, 5-Br-dUrd 5-bromodeoxyuridine, 5-Cl-dUrd 5-chlorodeoxyuridine, dFdU 2',2'-difluorodeoxyuridine, (-)Carbovir (C-D4G), 2,6-Diamino-ddP (ddDAPR; DAPDDR; 2,6-Diamino-2',3'-dideoxypurine-9-ribofuranoside), 9-(2'-Azido-2',3'-dideoxy- β -D-erythro-pentofuranosyl)adenine (2'-Azido-2',3'-dideoxyadenosine; 2'-N3ddA), 2'-FddT (2'-Fluoro-2',3'-dideoxy- β -D-erythro-pentofuranosyl)thymine), 2'-N3ddA(β -D-threo) (9-(2'-Azido-2',3'-dideoxy- β -D-threopentofuranosyl)adenine), 3-(3-Oxo-1-propenyl)AZT (3-(3-Oxo-1-propenyl)-3'-azido-3'-deoxythymidine), 3'-Az-5-Cl-ddC (3'-Azido-2',3'-dideoxy-5-chlorocytidine), 3'-N3-3'-dT (3'-Azido-3'-deoxy-6-azathymidine), 3'-F-4-Thio-ddT (2',3'-Dideoxy-3'-fluoro-4-thiothymidine), 3'-F-5-Cl-ddC (2',3'-Dideoxy-3'-fluoro-5-chlorocytidine), 3'-FddA (B-D-Erythro) (9-(3'-Fluoro-2',3'-dideoxy-B-D-erythropenta-furanosyl)adenine), Uravidine (3'-Azido-2',3'-dideoxyuridine; AzdU), 3'-FddC (3'-Fluoro-2',3'-dideoxycytidine), 3'-F-ddDAPR (2,6-Diaminopurine-3'-fluoro-2',3'-dideoxyriboside), 3'-FddG (3'-Fluoro-2',3'-dideoxyguanosine), 3'-FddU (3'-Fluoro-2',3'-dideoxyuridine), 3'-Hydroxymethyl-ddC (2',3'-Dideoxy-3'-hydroxymethyl cytidine; BEA-005), 3'-N3-5-CF3-ddU (3'-Azido-2',3'-dideoxy-5-trifluoromethyluridine), 3'-N3-5-Cyanomethoxy-ddU (3'-Azido-2',3'-dideoxy-5-[(cyanomethyl)oxy]uridine), 3'-N3-5-F-ddC (3'-Azido-2',3'-dideoxy-5-fluorocytidine), 3'-N3-5-Me-ddC (CS-92; 3'-Azido-2',3'-dideoxy-5-methylcytidine), 3'-N3-5-NH2-ddU (3'-Azido-2',3'-dideoxy-5-aminouridine), 3'-N3-5-NHMe-ddU (3'-Azido-2',3'-dideoxy-5-methyaminouridine), 3'-N3-5-NMe2-ddU (3'-Azido-2',3'-dideoxy-5-dimethylaminouridine), 3'-N3-5-OH-ddU (3'-Azido-2',3'-dideoxy-5-hydroxyuridine), 3'-N3-5-SCN-ddU (3'-Azido-2',3'-dideoxy-5-thiocyanatouridine), 3'-N3-ddA (9-(3'-Azido-2',3'-dideoxy-B-D-erythropenta-furanosyl)adenine), 3'-N3-ddC (CS-91; 3'-Azido-2',3'-dideoxycytidine), 3'-N3ddG (AZG; 3'-Azido-2',3'-dideoxyguanosine), 3'-N3-N4-5-diMe-ddC (3'-Azido-2',3'-dideoxy-N4--5-dimethylcytidine), 3'-N3-N4-OH-5-Me-ddC (3'-Azido-2',3'-dideoxy-N4-OH-5-methylcytidine), 4'-Az-3'-dT (4'-Azido-3'-deoxythymidine), 4'-Az-5ClU (4'-Azido-5-chloro-2'-deoxyuridine), 4'-AzdA (4'-Azido-2'-deoxyadenosine), 4'-AzdC (4'-Azido-2'-deoxycytidine), 4'-AzdG (4'-Azido-2'-deoxyguanosine), 4'-AzdI (4'-Azido-2'-deoxyinosine), 4'-AzdU (4'-Azido-2'-deoxyuridine), 4'-Azidothymidine (4'-Azido-2'-deoxy-.beta.-D-erythro-pentofuranosyl-5-methyl-2,4-dioxopyrimidine), 4'-CN-T (4'-Cyanothymidine), 5-Et-ddC (2',3'-Dideoxy-5-ethylcytidine), 5-F-ddC (5-Fluoro-2',3'-Cyanothymidine)

dideoxycytidine), 6Cl-ddP (D2CIP; 6-Chloro-ddP; CPDDR; 6-Chloro-9-(2,3-dideoxy-.beta.-D-glyceropentofuranosyl)-9H-purine), 935U83 (2',3'-Dideoxy-3'-fluoro-5-chlorouridine; 5-Chloro-2',3'-dideoxy-3'-fluorouridine; FddCIU; Raluridine), AZddBrU (3'-N3-5-Br-ddU; 3'-Azido-2',3'-dideoxy-5-bromouridine), AzddCIU; AzddCIUrd (3'-Azido-5-chloro-2',3'-dideoxyuridine), AZddEtU (3'-N3-5-EtddU; CS-85; 3'-Azido-2',3'-dideoxy-5-ethyluridine), AZddFU (3'-Azido-2',3'-dideoxy-5-fluorouridine), AZddIU (3'-N3-5-I-ddU; 3'-Azido-2',3'-dideoxy-5-iodouridine), AZT-2,5'-anhydro (2,5'-Anhydro-3'-azido-3'-deoxythymidine), AZT- α -L (α -L-AZT), AZU-2,5'-anhydro (2,5'-Anhydro-3'-azido-2',3'-dideoxyuridine), C-analog of 3'-N3-ddU (3'-Azido-2',3'-dideoxy-5-aza-6-deazauridine), D2SMeP (9-(2,3-Dideoxy- β -D-ribofuranosyl)-6-(methylthio)purine), D4A (2',3'-Dideoxydidehydroadenosine), D4C (2',3'-Didehydro-3'-deoxycytidine), D4DAP (2,6-Diaminopurine-2',3'-dideoxydidehydroriboside; ddeDAPR), D4FC (D-D4FC; 2',3'-Didehydro-2',3'-dideoxy-5-fluorocytidine), D4G (2',3'-Didehydro-2',3'-dideoxyguanosine), DMAPDDR (N-6-dimethyl ddA; 6-Dimethylaminopurine-2',3'-dideoxyriboside), dOTC (-) ((-)-2'-Deoxy-3'-oxa-4'-thiocytidine), dOTC (+) ((+)-2'-Deoxy-3'-oxa-4'-thiocytidine), dOTFC (-) ((-)-2'-Deoxy-3'-oxa-4'-thio-5-fluorocytidine), dOTFC (+) ((+)-2'-Deoxy-3'-oxa-4'-thio-5-fluorocytidine), DXG ((-)- β -Dioxolane-G), DXC- α -L-(α -L-Dioxalane-C), FddBrU (2',3'-Dideoxy-3'-fluoro-5-bromouridine), FddIU (3'-Fluoro-2',3'-dideoxy-5-iodouridine), FddT (Alovudine; 3'-FddT; FddThD; 3'-FLT; FLT), FTC (Emtricitabine; Coviracil; (-)-FTC; (-)-2',3'-Dideoxy-5-fluoro-3'-thiacytidine), FTC- α -L- (α -L-FTC), L-D4A (L-2',3'-Didehydro-2',3'-dideoxyadenosine), L-D4FC (L-2',3'-Didehydro-2',3'-dideoxy-5-fluorocytidine), L-D4I (L-2',3'-Didehydro-2',3'-dideoxyinosine), L-D4G (L-2',3'-Didehydro-2',3'-deoxyguanosine), L-FddC (β -L-5F-ddC), Lodenosine (F-ddA; 2'-FddA (B-D-threo); 2'-F-dd-ara-A; 9-(2'-Fluoro-2',3'-dideoxy-B-D-threopenta-furanosyl)adenine), MeAZddIsoC (5-Methyl-3'-azido-2',3'-dideoxyisocytidine), N6-Et-ddA (N-Ethyl-2',3'-dideoxyadenosine), N-6-methyl ddA (N6-Methyl-2',3'-dideoxyadenosine) or RO31-6840 (1-(2',3'-Dideoxy-2'-fluoro- β -D-threo-pentofuranosyl)cytosine).

27. The composition according to any of the preceding claims wherein the nucleoside analog is cytidine analog, a guanosine analog or an adenosine selected from the group consisting of dFdC gemcitabine (2',2'-difluorodeoxycytidine), 2-chloro-2'-deoxyadenosine (2CdA), CaFdA (2-chloro-2-ara-fluoro-deoxyadenosine), fludarabine (2-Fluoroadenine 9-beta-D-Arabinofuranoside), 2',3'-dideoxycytidine (ddC), 2',3'-dideoxyadenosine (ddA), 2',3'-dideoxyguanosine (ddG), ara-A (adenosine-arabinoside; Vivarabine), ara-C (cytidine-arabinoside), ara-G (9-beta-D-arabinofuranosylguanine), aciclovir (9-[2-hydroxy-ethoxy]-methyl-guanosine), buciclovir, famciclovir, ganciclovir (9-

[2-hydroxy-1-(hydroxymethyl)ethoxyl-methyl]-guanosine), penciclovir, valciclovir, 3TC (2'-deoxy-3'-thiacytidine), dFdG (2',2'-difluorodeoxyguanosine), 2,6-Diamino-ddP (ddDAPR; DAPDDR; 2,6-Diamino-2',3'-dideoxypurine-9-ribofuranoside), 9-(2'-Azido-2',3'-dideoxy- β -D-erythropentofuranosyl)adenine (2'-Azido-2',3'-dideoxyadenosine; 2'-N3ddA), 2'-N3ddA(β -D-threo) (9-(2'-Azido-2',3'-dideoxy- β -D-threopentofuranosyl)-adenine), 3'-Az-5-Cl-ddC (3'-Azido-2',3'-dideoxy-5-chlorocytidine), 3'-F-5-Cl-ddC (2',3'-Dideoxy-3'-fluoro-5-chlorocytidine), 3'-FddA (B-D-Erythro) (9-(3'-Fluoro-2',3'-dideoxy-B-D-erythropentafuranosyl)adenine), 3'-FddC (3'-Fluoro-2',3'-dideoxycytidine), 3'-F-ddDAPR (2,6-Diaminopurine-3'-fluoro-2',3'-dideoxyriboside), 3'-FddG (3'-Fluoro-2',3'-dideoxyguanosine), 3'-Hydroxymethyl-ddC (2',3'-Dideoxy-3'-hydroxymethyl cytidine; BEA-005), 3'-N3-5-F-ddC (3'-Azido-2',3'-dideoxy-5-fluorocytidine), 3'-N3-5-Me-ddC (CS-92; 3'-Azido-2',3'-dideoxy-5-methylcytidine), 3'-N3-ddA (9-(3'-Azido-2',3'-dideoxy-B-D-erythropentafuranosyl)adenine), 3'-N3-ddC (CS-91; 3'-Azido-2',3'-dideoxycytidine), 3'-N3ddG (AZG; 3'-Azido-2',3'-dideoxyguanosine), 3'-N3-N4-5-diMe-ddC (3'-Azido-2',3'-dideoxy-N4--5-dimethylcytidine), 3'-N3-N4-OH-5-Me-ddC (3'-Azido-2',3'-dideoxy-N4-OH-5-methylcytidine), 4'-AzdA (4'-Azido-2'-deoxyadenosine), 4'-AzdC (4'-Azido-2'-deoxycytidine), 4'-AzdG (4'-Azido-2'-deoxyguanosine), 5-Et-ddC (2',3'-Dideoxy-5-ethylcytidine), 5-F-ddC (5-Fluoro-2',3'-dideoxycytidine), 6Cl-ddP (D2CIP; 6-Chloro-ddP; CPDDR; 6-Chloro-9-(2,3-dideoxy-.beta.-D-glyceropentofuranosyl)-9H-purine), D2SMeP (9-(2,3-Dideoxy- β -D-ribofuranosyl)-6-(methylthio)purine), D4A (2',3'-Dideoxydidehydroadenosine), D4C (2',3'-Didehydro-3'-deoxycytidine), D4DAP (2,6-Diaminopurine-2',3'-dideoxydidehydroriboside; ddeDAPR), D4FC (D-D4FC; 2',3'-Didehydro-2',3'-dideoxy-5-fluorocytidine), D4G (2',3'-Didehydro-2',3'-dideoxyguanosine), DMAPDDR (N-6-dimethyl ddA; 6-Dimethylaminopurine-2',3'-dideoxyriboside), dOTC (-) ((-)2'-Deoxy-3'-oxa-4'-thiacytidine), dOTC (+) ((+)-2'-Deoxy-3'-oxa-4'-thiacytidine), dOTFC (-) ((-)2'-Deoxy-3'-oxa-4'-thio-5-fluorocytidine), dOTFC (+) ((+)-2'-Deoxy-3'-oxa-4'-thio-5-fluorocytidine), DXG ((-) β -Dioxolane-G), DXC- α -L-(α -L-Dioxalane-C), FTC (Emtricitabine; Coviracil; (-)-FTC; (-)-2',3'-Dideoxy-5-fluoro-3'-thiacytidine), FTC- α -L- (α -L-FTC), L-D4A (L-2',3'-Didehydro-2',3'-dideoxyadenosine), L-D4FC (L-2',3'-Didehydro-2',3'-dideoxy-5-fluorocytidine), L-D4I (L-2',3'-Didehydro-2',3'-dideoxyinosine), L-D4G (L-2',3'-Didehydro-2',3'-deoxyguanosine), L-FddC (β -L-5F-ddC), Lodenosine (F-ddA; 2'-FddA (β -D-threo); 2'-F-dd-ara-A; 9-(2'-Fluoro-2',3'-dideoxy-B-D-threopentafuranosyl)adenine), MeAZddIsoC (5-Methyl-3'-azido-2',3'-dideoxyisocytidine), N6-Et-ddA (N-Ethyl-2',3'-dideoxyadenosine), N-6-methyl ddA (N6-Methyl-2',3'-dideoxyadenosine) or RO31-6840 (1-(2',3'-Dideoxy-2'-fluoro- β -D-threopentofuranosyl)cytosine).

28. The composition according to any of the preceding claims, wherein the at least one nucleoside analogue is selected from the group consisting of D4T, ddC, AZT, ACV, 5 3TC, ddA Fludarabine, Cladribine, araC, gemcitabine, Clofarabine, Nelarabine (araG), and Ribavirin.

29. The composition according to any of the preceding claims, wherein the at least one nucleoside analogue is gemcitabine or AZT.

10 30. The composition according to any of the preceding claims, comprising at least two nucleoside analogues, such as at least 3 nucleoside analogues, for example at least 4 nucleoside analogues, such as at least 5 nucleoside analogues.

15 31. The composition according to any of the preceding claims, comprising at least three compounds capable of enhancing gap-junction communication, such as at least 3 compounds, for example at least 4 compounds, such as at least 5 compounds.

20 32. A method of treating cancer comprising administering to a patient in need thereof a therapeutically effective amount of at least one compound capable of increasing gap-junction communication, and at least one nucleoside analogue.

33. The method of claim 32, further comprising administering a source of deoxyribonucleoside kinase.

25 34. The method of claim 32, wherein the cancer is a multicellular cancer type.

35. The method of claim 33, wherein the cancer is selected from the group consisting of glioblastoma, bladder cancer, neuroblastoma, esophageal cancer, tongue cancer, hepatocellular carcinoma, lung cancer, malignant melanoma, ovarian cancer, prostate 30 cancer, renal cell carcinoma, and breast cancer.

36. The method of claim 35, wherein the cancer is breast cancer or glioblastoma.

37. The method of claim 33, wherein the deoxyribonucleoside kinase is administered to the 35 cancer cells using a gene therapy vector.

38. The method of claim 37, wherein the gene therapy vector is a virus vector selected from the group consisting of Herpes simplex viral vector, adenoviral vector, adenovirus-associated viral vector, lentiviral vector, retroviral vector, and a vaccinia viral vector.
- 5 39. The method of claim 38, wherein the gene therapy vector is administered to the cancer cells by implanting a composition of packaging cells capable of producing an infective virion comprising the viral vector.
- 10 40. The method of claim 39, wherein the packaging cells are encapsulated, and/or wherein the packaging cells are attached to a support matrix.
41. The method of claim 37, wherein the gene therapy vector is a plasmid vector.
- 15 42. The method of claim 41, wherein the plasmid vector is selected from the group consisting of general eukaryotic expression vectors, vectors for stable and transient expression and epitag vectors as well as their TOPO derivatives for fast cloning of desired inserts.
- 20 43. The method of claim 33, wherein the thymidine kinase is administered to the cancer cells by implanting a composition of human stem or precursor/progenitor cells, comprising a heterologous expression construct capable of expressing said deoxyribonucleoside kinase, and wherein said human stem cells are capable of forming a tight junction with cells in the tumour.
- 25 44. The method of claim 43, wherein said human stem or precursor/progenitor cells are human neural stem or precursor/progenitor cells.
45. The method of any of the preceding claims 32 to 44, comprising administration of the composition of any of the preceding claims 1 to 31.
- 30 46. The method of any of the preceding claims 32 to 44, wherein said compound capable of enhancing gap-junction communication is 4-phenylbutyrate, or a pharmaceutically acceptable salt thereof.
47. Use of at least one compound capable of enhancing gap-junction communication, and at least one nucleoside analogue, for the preparation of a medicament for the treatment of cancer.

48. The use of claim 47, further comprising a source of deoxyribonucleoside kinase.
49. The use of claim 48, wherein the source of deoxyribonucleoside kinase comprises a gene therapy vector capable of transducing at least a fraction of the cancer cells.
50. The use of claim 48, wherein the source of deoxyribonucleoside kinase comprises a composition of packaging cells capable of producing an infective virion comprising a viral gene therapy vector.
51. The use of claim 48, wherein the source of deoxyribonucleoside kinase comprises a protein formulation.
52. The use of claim 48, wherein the source of deoxyribonucleoside kinase comprises human stem cells, genetically modified to overexpress a deoxyribonucleoside kinase capable of converting said prodrug into a cytotoxic drug.
53. The use of claim 47, wherein the cancer is a multicellular, solid tumor.
54. The use of claim 53, wherein the cancer is selected from the group consisting of glioblastoma, bladder cancer, neuroblastoma, esophageal cancer, tongue cancer, hepatocellular carcinoma, lung cancer, malignant melanoma, ovarian cancer, prostate cancer, renal cell carcinoma, and breast cancer.
55. The use of claim 54, wherein the cancer is breast cancer or glioblastoma.
56. The use of claim 48, wherein said medicament comprises the composition according to any of the preceding claims 1 to 31.
57. The use of claim 48, wherein said medicament comprises 4-phenylbutyrate or a pharmaceutically acceptable salt thereof.
58. A method of augmenting the therapeutic activity of a nucleoside analogue based cancer therapy, said method comprising administering to a patient an amount of at least one compound capable of enhancing gap-junction communication and thereby augmenting the therapeutic activity of said nucleoside analogue based therapy.

59. The method of claim 58, wherein said nucleoside analogue based therapy further comprises administration of a source of deoxyribonucleoside kinase.
60. The method of claim 58, wherein said compound capable of enhancing gap-junction communication is 4-phenylbutyrate or a pharmaceutically acceptable salt thereof.
61. The method of claim 58, comprising administering the composition according to any of the preceding claims 1 to 31.
- 10 62. Pharmaceutical articles containing at least one nucleoside analogue and at least one compound capable of enhancing gap-junction communication as a combination for the simultaneous, separate or successive administration in cancer therapy.
63. Articles of claim 62, further comprising a source of deoxyribonucleoside kinase.
- 15 64. Articles of claim 62, wherein said compound capable of enhancing gap-junction communication is 4-phenylbutyrate or a pharmaceutically acceptable salt thereof.
65. Articles of claim 62, comprising the composition according to any of the preceding
20 claims 1 to 31.
66. Articles of claim 62, wherein the cancer is a multicellular cancer type.
67. Articles of claim 62, wherein the cancer is selected from the group consisting of
25 glioblastoma, bladder cancer, neuroblastoma, esophageal cancer, tongue cancer, hepatocellular carcinoma, lung cancer, malignant melanoma, ovarian cancer, prostate cancer, renal cell carcinoma, and breast cancer.
68. Articles of claim 62, wherein the cancer is breast cancer or glioblastoma.